ORIGINAL ARTICLE

EFFECT OF THYROID HORMONE REPLACEMENT ON RESPIRATORY FUNCTION TESTS IN HYPOTHYROID WOMEN

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Background: Respiratory system, like other body systems and organs, is affected by hypothyroidism. Many patients of hypothyroidism complain of fatigue and exercise intolerance. These might be due to limited pulmonary reserve. This study was carried out to observe FVC, FEV_1, FEV_1/FVC and PEF in hypothyroid Punjabi women grouped on the basis of duration of treatment received. **Methods:** Twenty-six recently diagnosed hypothyroid women (Group-A), and 22 hypothyroid women taking medication for the last 6–8 months (Group-B) were subjected to estimation of FVC, FEV_1, FEV_1/FVC and PEF and compared with 25 apparently euthyroid subjects (Group-C). They were also assessed for serum T_4 and serum TSH. Data were analysed by One-way ANOVA with Post-Hoc Tukey HSD and Pearson's correlation. **Results:** The mean values for FVC, FEV_1 and PEF were more in treated hypothyroid subjects and euthyroid controls compared to untreated hypothyroid patients and the differences were highly significant ($p<0.001$), although no significant correlation could be derived between serum T_4, serum TSH, and the pulmonary parameters. **Conclusion:** In hypothyroid women, there was a significant difference in the lung functions between those not taking any treatment and those on thyroid hormone replacement therapy. Lung functions can be used as a tool to assess the effectiveness of treatment of hypothyroidism.

Keywords: forced vital capacity, FEV_1, peak expiratory flow, T_4 thyroxin, TSH, thyroid stimulating hormone, hypothyroid, women, euthyroid

INTRODUCTION

Hypothyroidism is relatively a common disease worldwide. Thyroid hormone deficiency has been linked to increased risk of cardiovascular morbidities and mortalities.[1] Hypothyroidism affects all of the organ systems. Clinical findings include fatigue, dryness of the skin, cold intolerance, weight gain without loss of appetite, constipation, swelling of the extremities, dyspnoea, hoarseness of speech, menorrhagia, hair loss, bradycardia and multiple neurological symptoms (like paraesthesia, hearing disorders, delayed relaxation of tendon reflexes, carpal tunnel syndrome, lack of concentration and amnesia).[2] All of these signs and symptoms recover after replacement of thyroid hormone.[3]

Respiratory system like other body systems and organs is affected by hypothyroidism. The spectrum of diseases involvement can range from mild dyspnoea to more severe and life threatening respiratory failure.[4,5] Hypothyroidism exerts different effects on the respiratory system. One of the major effects of hypothyroidism is its influence on the central ventilatory control. Hypoxic ventilatory drive is significantly depressed in both untreated myxoedema and during brief periods of thyroid hormone insufficiency. This depression is particularly striking in myxoedema. Hypoxic ventilatory drive increases dramatically with hormone replacement therapy.[6,7] Hypothyroidism may lead to the development of myopathy, and has been evaluated particularly for the inspiratory and expiratory muscles. Inspiratory and expiratory muscle strength is linearly related to the degree of hypothyroidism and suppletion restores respiratory muscle function.[8] Majority of systemic effects are present due to reduction in metabolic activity and deposition of glycosaminoglycans in interstitial tissues.[9] Several researchers reported that pulmonary functions may decrease in hypothyroid females and after thyroid hormone replacement these values may increase significantly in these groups of patients.[10–13] Many patients with hypothyroidism complain of fatigue and exercise intolerance. These subjective sensations could arise from limited pulmonary reserve, limited cardiac reserve, decreased muscle strength or increased ease of muscle fatigue.[14] Dyspnoea, as a subjective sensation, is prevalent in hypothyroidism, seems to be secondary to limited pulmonary reserve or limited cardiac reserve.[15] The incidence of hypothyroidism is greater in women than men with a ratio of 5:1.[16]

The present study was designed to determine the probable abnormalities in pulmonary function tests of hypothyroid women and to evaluate the effect of thyroid hormone therapy in such patients.

MATERIAL AND METHODS

This cross-sectional study was carried out in the Department of Physiology, Sri Guru Ram Das Institute of Medical Sciences & Research

(SGRDIMSR), Amritsar, India. Twenty-six recently diagnosed hypothyroid women in the age group 30–45 years were placed in Group-A. Another 22 hypothyroid women who were receiving treatment for hypothyroidism for the last 6–8 months were included in Group-B. Both groups were compared with 25 apparently euthyroid women who were matched for age, BMI and socioeconomic status and served as controls (Group-C). Subjects with serum T_4<5.53 µg/dl and serum TSH>4.68 mIU/L by Chemiluminiscence Method[17] were taken as hypothyroid. Subjects were selected from Outpatient Department (OPD) of Department of Medicine, SGRDIMSR. The controls were taken from the general population.

Subjects with history of any type of smoking, COPD, heart disease, diabetes mellitus, hypertension, chronic renal failure were excluded from the study. Subjects affected with any physiological condition which alters the pulmonary functions, were also excluded. They were examined at the Department of Physiology of the same institute. A detailed history including medical, personal, occupational, drug intake and socioeconomic status was taken. A complete physical examination was done which included measurement of height, weight and body surface area (BSA). Spirometry was done on all subjects on a PC based spirometer SPIROEXCEL™. The readings documented were that of FVC, FEV_1, FEV_1/FVC and PEF.

The data were analysed using One-way ANOVA with Post-Hoc Tukey HSD, and Pearson's correlation and inferences were drawn.

RESULTS

Table-1 shows the anthropometric parameters in the three groups. The mean values for weight showed highly significant differences between Group-A and Group-B, and Group-A and Group-C (p<0.001); and a non-significant difference between Group-B and Group-C. The mean values for body surface area (BSA) also showed a highly significant difference between Group-A and Group-B and a significant difference (p<0.05) between Group-A and Group-C. However, the difference was non-significant between Group-B and Group-C. The mean values for BMI showed a highly significant difference between Group-A and Group-B, and Group-A and Group-C, while the differences between Group-B and Group-C were non-significant. The mean values for age and height did not show any significant differences between groups.

Spirometric variables in all the three groups are shown in Table-2. Spirometric parameters (FVC, FEV_1 and PEF), except for FEV_1/FVC showed a highly significant decrease in untreated hypothyroids compared to treated hypothyroids and euthyroid controls. The difference in values for FVC and FEV_1 were highly significant between Group-A and Group-B, and between Group-A and Group-C. The FEV_1/FVC did not show any significant difference in any of the groups. The values for PEF showed a highly significant difference in all the groups. The mean values for serum TSH were significantly higher in Group-A than Group-B and Group-C. It also shows that the mean values for serum T_4 were significantly lower in Group-A compared to Group-B and Group-C. The difference in serum TSH was statistically significant between Group-A and Group-B, Group-A and Group-C, and Group-B and Group-C. The differences in serum T4 values were statistically significant between Group-A and Group-B, Group-A and Group-C, and Group-B and Group-C.

The spirometric variables when correlated with serum TSH and serum T_4 did not show any significant changes. The r-value for FEV_1 was highly significant negatively in Group-A. Similarly, r-value for FEV_1/FVC was highly significant negatively in Group-A. The r-value for PEF was highly significant negatively in Group-B. Rest of the r-values were not statistically significant.

Table-1: Anthropometric data of the subjects

	Group-A (n=26)	Group-B (n=22)	Group-C (n=25)	Group A vs B#	Group A vs C#	Group B vs C#
Age (Year)	39.81±2.07	41.77±4.82	40.68±3.50	0.146	0.659	0.550
Weight(Kg)	67.27±5.64	58.36±5.38	59.32±4.06	<0.001**	<0.001**	0.796
Height(Cm)	156.81±5.50	155.36±4.99	157.92±6.04	0.644	0.755	0.263
BSA (m^2)	1.67±0.09	1.56±0.08	1.59±0.08	<0.001**	0.005*	0.455
BMI (Kg/m^2)	27.34±1.06	24.19±2.21	23.81±1.61	<0.001**	<0.001**	0.753

#p using One-Way ANOVA with Post-Hoc Tukey HSD, *p<0.05=Significant, **p<0.001=Highly significant

Table-2: Spirometry variables, TSH and T_4 in the groups

	Group-A (n=26)	Group-B (n=22)	Group-C (n=25)	Group A vs B#	Group A vs C#	Group B vs C#
FVC (L)	2.31±0.48	2.76±0.40	2.91±0.31	0.065	<0.001**	<0.001**
FEV_1 (L)	1.72±0.328	2.12±0.28	2.33±0.24	0.412	<0.001**	<0.001**
FEV_1/FVC (%)	76.6±0.17	78.5±0.17	81.09±0.12	0.523	0.317	0.946
PEF (L/sec)	2.89±0.46	3.50±0.36	4.84±0.36	<0.001**	<0.001**	<0.001**
TSH (m IU/L)	14.12±2.14	7.04±1.05	1.46±0.40	<0.001**	<0.001**	<0.001**
T_4(µ/dl)	2.02±0.64	9.18±0.81	10.23±0.52	<0.001**	<0.001**	<0.001**

#p using One-Way ANOVA with Post-Hoc Tukey HSD, **p<0.001=Highly significant

Table-3: Pearson correlation coefficients (*r*) between spirometric variables and TSH/T_4

	TSH (mIU/L)			T_4 (µg/dL)		
	Group-A (n=26)	Group-B (n=22)	Group-C (n=25)	Group-A (n=26)	Group-B (n=22)	Group-C (n=25)
FVC (L)	0.221	0.046	-0.242	0.118	0.132	-0.249
FEV_1 (L)	-0.530**	0.065	0.284	-0.031	-0.059	-0.177
FEV_1/FVC (%)	-0.415**	-0.011	0.342	-0.122	-0.142	0.040
PEF (L/sec)	0.109	-0.817*	-0.006	-0.084	-0.146	0.141

*p<0.01: Significant

DISCUSSION

Respiratory system components (respiratory centre, upper airway and lower respiratory system) can be affected by deficiencies in body hormones as well as excess hormonal secretion.[18–21] Thyroid hormone is one of the major body hormones. Its deficiency has been associated with multiple cardiovascular complications, respiratory failure and coma.[4,22–24] Hypothyroidism is associated with diminished ventilatory drive for both hypoxia and hypercapnia.[25]

Both inspiratory and expiratory respiratory muscles are weakened in hypothyroidism in a direct linear relationship to the thyroid hormone level and it is reversible with thyroxinetherapy.[8] Furthermore, thyroid deficient muscles have impaired free fatty acid utilisation, which enhances their glycogen consumption, thereby reducing skeletal muscle endurance. One of the major inspiratory muscles that are involved in hypothyroidism is the diaphragm.[26] Diaphragm weakness can be very severe and associated with hypoventilation.[27]

In our study, we found that the values for FVC and FEV_1 were significantly lower in recently diagnosed hypothyroids as compared to treated hypothyroids and apparently euthyroids. These findings are supported by studies by other researchers.[11,12] But the same parameters were not significantly decreased between the treated hypothyroids and the apparently euthyroids which is in concordance with certain other studies.[7,8,10] The ratio FEV_1/FVC did not show any significant difference between all the three groups as observed by another group of researchers.[6,9,10] The values for PEF showed a significant difference between all the three groups which is supported by a similar study.[11] Some patients with hypothyroidism have alveolar hypoventilation. Frequently reported findings include decreased vital capacity, FEV_1, FVC, and total lung capacity, which some authors have explained as occurring through alveolar hypoventilation and inspiratory muscle power weakness.[27,28]

The changes observed in our spirometric findings can be explained on the basis of researches by some investigators which suggest that respiratory centre depression, interference of neural conduction or neuromuscular transmission to the respiratory muscles and respiratory muscles diseases in hypothyroidism may cause alveolar hypoventilation which may affect central ventilatory control and can impair ventilation.[29] In addition, in hypothyroidism, reduced surfactant phospholipid, phosphatidylglycerol and phosphatidic acid along with increase in surface active lipids phosphatidylserine and phosphatidylinositol in alveolar epithelium may decrease alveolar septation and reduce lung compliance and surfactant adsorption.[30–33] Moreover, mucopolysaccharide deposition in the lungs may cause fibrosis and thickening of the alveolar wall with loss of elastic tissue and may increase the work of breathing. All these changes may reduce ventilatory lung functions.[34]

Respiratory infections are more common in hypothyroid patients than healthy people which might be the cause of low PFT parameters.[35,36] Another study showed that hypothyroidism could cause restrictive changes in respiratory system that are reversible after treatment with levothyroxin. These changes are more significant in females of older ages.[10] Respiratory muscle strength is reduced in patients with hypothyroidism, and improves with treatment; the reduction is caused by both myopathy and neuropathy. In a study on six patients, maximal expiratory and inspiratory pressures were reduced and improved with treatment.[37]

In our study, the decreased values for FVC, FEV_1 and PEF in untreated hypothyroid females as compared to treated hypothyroids and healthy controls can be attributed to low serum T_4 which may cause respiratory muscle weakness and decreased contractile strength. Low thyroid hormone levels also decrease lung elastic tissue and increase the work of breathing. The proportionate decrease in both FVC and FEV_1 resulted in no significant changes in FEV_1/FVC ratio. The treated hypothyroids showed significant changes in pulmonary functions after hormone replacement therapy as compared to untreated hypothyroids though significant correlation could be drawn between few spirometry variables and serum TSH but none was seen between spirometry variables and serum T_4.

CONCLUSION

A fall in thyroid hormone level in hypothyroidism can cause a decrease in pulmonary functions. This fall is responsive to hormone replacement therapy. Spirometric studies can be used for evaluating the effectiveness of treatment of hypothyroidism.

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